HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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Speech Abstracts

Abstract 001

POEMS SYNDROME: CLINICAL FEATURES, DIAGNOSIS, AND TREATMENT APPROACHES

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POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, Skin changes) is a rare paraneoplastic syndrome with multisystem involvement [1]. It typically arises from monoclonal plasma cell proliferation and is considered an atypical variant of multiple myeloma [2]. In the pathogenesis of the disease, markedly elevated levels of vascular endothelial growth factor (VEGF) play a crucial role, and most of the symptoms are associated with this mechanism [3]. The clinical presentation of POEMS syndrome is quite heterogeneous. In most patients, the polyneuropathy is a subacute, distal, sensorimotor and progressive demyelinating neuropathy; motor involvement is often prominent and significantly impairs patients' quality of life [4]. Organomegaly particularly hepatomegaly, splenomegaly, and lymphadenopathy is commonly observed. Endocrinopathy may present with a wide spectrum of disorders, including diabetes mellitus, hypothyroidism, and hypogonadism. Monoclonal gammopathy frequently of the λ (lambda) light chain type is a critical diagnostic finding. Cutaneous manifestations may include hyperpigmentation, hemangiomas, excessive hair growth (hypertrichosis), and skin thickening. Additional features can include papilledema, edema, ascites, pulmonary hypertension, and thromboembolic events [5,6]. The diagnostic criteria were first defined by Dispenzieri and colleagues and are currently based on a system of 'major and minor criteria.' For diagnosis, in addition to the two mandatory major criteria (polyneuropathy and monoclonal plasma cell proliferation), at least one additional major criterion and one minor criterion must be present. Measurement of VEGF levels is an important biomarker both for diagnosis and for monitoring treatment response [5]. Treatment is aimed at eliminating the underlying clonal plasma cell population. In patients with localized bone lesions, radiotherapy may be effective particularly in cases of limited disease. For widespread disease, systemic therapies are preferred. Immunomodulatory agents such as lenalidomide and thalidomide, as well as bortezomib based regimens, have been found effective. Autologous hematopoietic stem cell transplantation (HSCT) can provide long-term remission in suitable patients. Monitoring treatment response via VEGF levels shows that reductions in VEGF parallel clinical improvement [7,8]. Prognosis has markedly improved with treatment. Contemporary approaches have increased the 5-year survival rate to approximately 60–70%. However, delayed diagnosis—due to frequent misattribution of symptoms to other neurological or endocrine disorders—is a significant issue at presentation. Therefore, multidisciplinary collaboration among hematologists, neurologists, and endocrinologists is critical for timely diagnosis and effective treatment [9]. In conclusion, POEMS syndrome is a rare but clinically highly complex disorder. Early diagnosis and appropriate treatment improve both survival and quality of life. Given the syndrome's clinical heterogeneity, increasing awareness especially within hematology practice is of great value [10].

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Abstract 002

UPDATES ON TARGETED THERAPIES IN ACUTE MYELOID LEUKEMIA

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Acute myeloid leukemia (AML) is a malignant disease of bone marrow stem cells that can be fatal with current treatment methods. The median age of patients is 68, and a substantial proportion of cases are attributable to geriatric patients.

Following the administration of induction chemotherapy, complete remission (CR) is observed in approximately 73% - 45% of patients in the ELN-2022 favorable-adverse risk groups, respectively. However, overall survival (OS) and progression-free survival (PFS) are not satisfactory despite current treatments. The five-year PFS was estimated at 52% - 16%, and the five-year OS was 55% - 15%, respectively. As the pathogenesis of AML becomes clearer, clinical trials on current targeted therapies are increasing, and being developed to accompany or replace standard AML treatments that have been similar for nearly 50 years. It is now evident that epigenetic-based treatments can lead to significant changes in the fundamental model that underpins therapeutic interventions. The combination of BCL2 inhibitor venetoclax with hypomethylating agents has significantly improved survival, particularly in elderly and unfit patients. Studies are ongoing to combine intensive therapies with induction and consolidation therapy. Three FLT3 inhibitors (midostaurin, gilteritinib, and quizartinib) have shown promising results in induction and consolidation therapies, salvage therapies, and follow-up therapies after allogeneic transplantation. A phase Ib-II trial of crenolinib, a potent type I second-generation FLT3 inhibitor, demonstrates that its use with intensive therapy in newly diagnosed AML patients under 60 years of age improves survival and results in higher rates of MRD negativity. In addition, ongoing trials are also evaluating the 7 + 3 + midostaurin versus 7 + 3 with gilteritinib (NCT04027309). Other targeted studies are ongoing with IDH inhibitors (ivosidenib and olutasidenib targeting IDH1 mutations; enasidenib targeting IDH2 mutations). Olutasidenib has been shown to provide better response rates and survival compared to ivosidenib in elderly, unfit patients, and combination with azacitidine also increases OS. Other promising studies for AML appear to be focused on menin inhibitors. The phase 1 trial of Revumenib (AUGMENT-101 trial) and Ziftomenib (KOMET-001 trial) (both studies in patients with KMT2A rearranged and NPM1m R/R AML) have yielded positive results, and phase 2 trials are eagerly awaited. A phase 1 trial evaluating a third oral Menin inhibitor, JNJ-75276617, results rates were similar to the other 2 inhibitors. Clinical trials are now ongoing these drugs in combination with additional low dose and high dose chemotherapy regimens (NCT05735184, NCT05886049). Another area is immunotherapy in AML. The success of allogeneic stem cell transplantation has demonstrated the potential for immunotherapy. Talacotuzumab and Pivekimab, targeted to CD123, appear to be particularly effective in relapsed-refractory (R/R) patients, and combination studies with FLAG-IDA are ongoing. Additionally, Tagraxofusp, a drug containing IL-3 ligand conjugated to the first 388 amino acids of diphtheria toxin, has been studied combination with Azacitidine/Venetoclax in newly diagnosed AML patients. MRD negativity was found in 71% of patients. Magrolimab, which acts on CD47, has promising results in patients with R/R AML. The potential of ongoing targeted therapies to provide new insights into the treatment of AML.

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Abstract 003

OLD TRADITIONS IN A NEW VILLAGE*... WHY ARE FACTORS STILL NECESSARY? CONTEMPORARY PARADİGMS İN HEMOPHILIA MANAGEMENT AND THE IRREPLACEABLE ROLE OF FACTOR REPLACEMENT

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Hemophilia is an X-linked recessive hereditary coagulation disorder characterized by a deficiency of factor VIII (hemophilia A) or factor IX (hemophilia B). Beginning in childhood, it constitutes a lifelong global health problem, associated with substantial morbidity, mortality, and treatment costs. While novel approaches—including gene therapies and non-factor-based biologic agents—are reshaping therapeutic strategies, factor replacement therapies remain the indispensable cornerstone of hemophilia management due to persistent clinical, biological, and economic limitations. **Gene Therapy:** Gene transfer techniques utilizing adeno-associated virus (AAV) vectors (e.g., valoctocogene roxaparvovec, etranacogene dezaparvovec) have shown promise in maintaining sustained factor levels in adults. However, in pediatric populations, hepatocyte proliferation inevitably leads to loss of transgene expression. In addition, immune responses, hepatotoxicity, and the inability to administer repeat dosing represent major barriers to safety and efficacy in children. Ethical concerns further complicate implementation. For these reasons, gene therapy does not appear to be a feasible treatment option for pediatric hemophilia in the near future. **Non–Factor-Based Agents:** Emicizumab, a bispecific antibody that mimics the bridging function of factor VIII, has significantly reduced bleeding frequency and revolutionized care, particularly in hemophilia A patients with inhibitors. Its subcutaneous administration enhances treatment adherence. Nevertheless, its inability to rapidly increase factor levels in emergencies such as major surgery or trauma is a critical limitation. Likewise, RNA interference (RNAi) therapies such as fitusiran and tissue factor pathway inhibitor (TFPI) inhibitors (concizumab, marstacimab) have shown encouraging results in clinical trials. However, thrombotic risks and uncertainties surrounding long-term safety restrict their use in pediatric populations. **Factor Replacement Therapy:** Standard and extended half-life (EHL) FVIII/FIX concentrates, supported by more than four decades of safety data, continue to form the foundation of prophylaxis in childhood. EHL products have reduced treatment burden with once- or twice-weekly dosing, while playing a vital role in maintaining joint health and preventing trauma-related bleeding episodes. Factor replacement therapy remains the gold standard for the management of acute bleeding. **Global Access and Health Economics:** Gene therapies and biologic agents are accessible almost exclusively in high-income countries due to their prohibitive costs (USD 2–3 million per treatment; emicizumab approximately USD 400,000 annually). In contrast, in low- and middle-